

PATENT COOPERATION TREATY

PCT

REC'D 17 JAN 2002

INTERNATIONAL PRELIMINARY EXAMINATION REPORT PCT

(PCT Article 36 and Rule 70)

Applicant's or agent's file reference 10662-99PCT	FOR FURTHER ACTION See Notification of Transmittal of International Preliminary Examination Report (Form PCT/IPEA/416)	
International application No. PCT/CA00/01142	International filing date (day/month/year) 03/10/2000	Priority date (day/month/year) 05/10/1999
International Patent Classification (IPC) or national classification and IPC A61K41/00		
Applicant UNIVERSITE DE MONTREAL et al.		

1. This international preliminary examination report has been prepared by this International Preliminary Examining Authority and is transmitted to the applicant according to Article 36.



2. This REPORT consists of a total of 6 sheets, including this cover sheet.

- ☒ This report is also accompanied by ANNEXES, i.e. sheets of the description, claims and/or drawings which have been amended and are the basis for this report and/or sheets containing rectifications made before this Authority (see Rule 70.16 and Section 607 of the Administrative Instructions under the PCT).

These annexes consist of a total of 6 sheets.

3. This report contains indications relating to the following items:

- I ☒ Basis of the report
- II ☐ Priority
- III ☒ Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- IV ☐ Lack of unity of invention
- V ☒ Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- VI ☐ Certain documents cited
- VII ☐ Certain defects in the international application
- VIII ☐ Certain observations on the international application

Date of submission of the demand 03/05/2001	Date of completion of this report 15.01.2002
Name and mailing address of the international preliminary examining authority:  European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 eprnu d Fax: +49 89 2399 - 4465	Authorized officer Toulacis, C Telephone No. +49 89 2399 8638 

INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No. PCT/CA00/01142

I. Basis of the report

1. With regard to the **elements** of the international application (*Replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this report as "originally filed" and are not annexed to this report since they do not contain amendments (Rules 70.16 and 70.17)*):

Description, pages:

1-40 as originally filed

Claims, No.:

1-16 as received on 20/12/2001 with letter of 20/12/2001

Drawings, sheets:

1/12-12/12 as originally filed

2. With regard to the **language**, all the elements marked above were available or furnished to this Authority in the language in which the international application was filed, unless otherwise indicated under this item.

These elements were available or furnished to this Authority in the following language: , which is:

- ☐ the language of a translation furnished for the purposes of the international search (under Rule 23.1(b)).
- ☐ the language of publication of the international application (under Rule 48.3(b)).
- ☐ the language of a translation furnished for the purposes of international preliminary examination (under Rule 55.2 and/or 55.3).

3. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international preliminary examination was carried out on the basis of the sequence listing:

- ☐ contained in the international application in written form.
- ☐ filed together with the international application in computer readable form.
- ☐ furnished subsequently to this Authority in written form.
- ☐ furnished subsequently to this Authority in computer readable form.
- ☐ The statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.
- ☐ The statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished.

4. The amendments have resulted in the cancellation of:

- ☐ the description, pages:
- ☐ the claims, Nos.:

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA00/01142

☐ the drawings, sheets:

5. ☐ This report has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed (Rule 70.2(c)):

(Any replacement sheet containing such amendments must be referred to under item 1 and annexed to this report.)

6. Additional observations, if necessary:

III. Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

1. The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application.

☒ claims Nos. 2-12, 15 and 16 with regard to industrial applicability; See separate sheet.

because:

☐ the said international application, or the said claims Nos. relate to the following subject matter which does not require an international preliminary examination (*specify*):

☐ the description, claims or drawings (*indicate particular elements below*) or said claims Nos. are so unclear that no meaningful opinion could be formed (*specify*):

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed.

☐ no international search report has been established for the said claims Nos. .

2. A meaningful international preliminary examination cannot be carried out due to the failure of the nucleotide and/or amino acid sequence listing to comply with the standard provided for in Annex C of the Administrative Instructions:

☐ the written form has not been furnished or does not comply with the standard.

☐ the computer readable form has not been furnished or does not comply with the standard.

V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N) Yes: Claims 2-16

**INTERNATIONAL PRELIMINARY
EXAMINATION REPORT**

International application No. PCT/CA00/01142

	No:	Claims	1
Inventive step (IS)	Yes:	Claims	2-16
	No:	Claims	1
Industrial applicability (IA)	Yes:	Claims	1, 13, 14
	No:	Claims	

2. Citations and explanations
see separate sheet

III

Claims 2-12, 15 and 16 relate to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(i) PCT).

V

Reference is made to the following documents:

D1: WO 96 07431 A (UNIV MONTREAL) 14 March 1996 (1996-03-14)

D2: PAL, PRABIR ET AL: "Phototoxicity of some bromine-substituted rhodamine dyes: synthesis, photophysical properties and application as photosensitizers" PHOTOCHEM. PHOTOBIOLOG. (1996), 63(2), 161-8, XP000979188

Claim 1

(N) A pharmaceutical composition comprising at least one photoactive rhodamine **derivative** as defined in claim 1 of the present application and at least a pharmaceutically acceptable carrier, is already disclosed in the documents D1 and D2 cited in the search report.

See D1: claim 7; according to claim 7 of D1 the photoactivable derivative is administered by instillation, injection and bloodstream diffusion.

Said administration can only take place in form of a pharmaceutical composition comprising a pharmaceutically acceptable carrier (e.g. water or buffer).

D2: Abstract, line 9 (A solution of 4,5-dibromohodamine in water does constitute a pharmaceutical composition) .

According to claim 1 of the present application a list of rhodamine derivatives are defined. However, photoactive derivatives thereof are also claimed (claim 1, lines 18-19). Thus, the photoactive derivatives disclosed in documents D1 and D2, are considered to fall within the scope of claim 1.

(IS) The question - Is there inventive step - only arises if there is novelty.

(IA) The industrial applicability of claim 1, is beyond any doubt.

Claims 2-16

- (N) The use of a photoactive derivative as defined in claim 1 of the present application in a treatment or method as defined in claims 2-16, is not disclosed in the documents cited in the search report.
- (IS) Documents D1 and D2 refer to the use of photosensitizing agents for the elimination of malignant or cancer cells, whereas the methods claimed according to the present application refer to the elimination of immunoreactive cells, and therefore the treatment of immunologic disorders.
Said use is not suggested by documents D1 and/or D2.
- (IA) The industrial applicability of claims 13 and 14 is given.
For the assessment of the present claims 2-12, 15 and 16 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

WE CLAIM:

1. A photoactivable pharmaceutical composition for the selective destruction and/or inactivation of immunologically reactive cells without substantially affecting the normal cells or causing systemic toxicity for the patient, said composition comprising at least one photoactivable rhodamine derivative selected from the group consisting of 4,5-dibromorhodamine 123 (2-(4,5-dibromo-6-amino-3-imino-3H-xanthen-9-yl)-benzoic acid methyl ester) hydrobromide; 4, 5-dibromorhodamine 110 (2-(4,5-dibromo-6-amino-3-imino-3H-xanthen-9-yl)-benzoic acid) ethyl ester hydrobromide; 4, 5-dibromorhodamine 110 (2-(4,5-dibromo-6-amino-3-imino-3H-xanthen-9-yl)-benzoic acid) octyl ester hydrobromide; 4,5-dibromorhodamine 110 (2-(4,5-dibromo-6-amino-3-imino-3H-xanthen-9-yl)-benzoic acid) n-butyl ester hydrobromide; Rhodamine B n-butyl ester (2-(6-diethyl amino-3-ethyl imino-3H-xanthen-9-yl)-benzoic acid) n-butyl diester hydrochloride; and photoactivable derivatives thereof; in association with a pharmaceutically acceptable carrier; whereby photoactivation of said derivatives induces cell killing while unactivated derivatives are substantially non-toxic to cells.

2. Use of the photoactivable derivatives of claim 1 for the photodynamic treatment for the selective destruction and/or inactivation of immunologically reactive cells without substantially affecting the normal cells or causing systemic toxicity for the patient, wherein appropriate intracellular levels of said derivatives are achieved and irradiation of a suitable wavelength and intensity is applied.

3. A method of prevention of graft-versus-host disease associated with allogeneic stem cell transplantation in a patient, which comprises the steps of:

- a) activating lymphocytes from a donor by mixing donor cells with host cells for a period of time sufficient for an immune reaction to occur;
- b) substantially eliminating the activated lymphocytes of step a) with photodynamic therapy using a therapeutic amount of a photoactivable composition of claim 1 under irradiation of a suitable wavelength; and
- c) performing allogeneic stem cell transplantation using the treated mix of step b).

4. A method for the treatment of immunologic disorder in a patient, which comprises the steps of:

- a) harvesting said patient's hematopoietic cells;
- b) ex vivo treating of the hematopoietic cells of step a) by photodynamic therapy using a therapeutic amount of a photoactivable composition of claim 1 under irradiation of a suitable wavelength; and
- c) performing graft infusion or autograft transplantation using the treated hematopoietic cells of step b).

5. The method of claim 4, wherein said immunologic disorder is selected from the group consisting of conditions in which self cells or donor cells react against host tissues or foreign targets, such as graft-

versus-host disease, graft rejection, autoimmune disorders and immunoallergic conditions.

6. The method of claim 4, wherein said hematopoietic cells is selected from the group consisting of bone marrow, peripheral blood, and cord blood mononuclear cells.

7. A method of evaluating transport mechanism of immune and/or malignant cells, which comprises using the photoactivable pharmaceutical composition of claim 1.

8. The method of claim 7, wherein said composition is evaluated by flow cytometry.

PATENT COOPERATION TREATY

PCT

NOTIFICATION OF ELECTION

(PCT Rule 61.2)

From the INTERNATIONAL BUREAU

To:

Commissioner
 US Department of Commerce
 United States Patent and Trademark
 Office, PCT
 2011 South Clark Place Room
 CP2/5C24
 Arlington, VA 22202
 ETATS-UNIS D'AMERIQUE

in its capacity as elected Office

Date of mailing (day/month/year) 26 June 2001 (26.06.01)	
International application No. PCT/CA00/01142	Applicant's or agent's file reference 12411-21PCT
International filing date (day/month/year) 03 October 2000 (03.10.00)	Priority date (day/month/year) 05 October 1999 (05.10.99)
Applicant ROY, Denis-Claude et al	

1. The designated Office is hereby notified of its election made:

☒ in the demand filed with the International Preliminary Examining Authority on:
 03 May 2001 (03.05.01)

☐ in a notice effecting later election filed with the International Bureau on:

2. The election ☒ was
☐ was not

made before the expiration of 19 months from the priority date or, where Rule 32 applies, within the time limit under Rule 32.2(b).

The International Bureau of WIPO 34, chemin des Colombettes 1211 Geneva 20, Switzerland Facsimile No.: (41-22) 740.14.35	Authorized officer Odile ALIU Telephone No.: (41-22) 338.83.38
--	---

INT. NATIONAL SEARCH REPORT

Ab. onal Application No

PCT/CA 95/00485

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHEMICAL ABSTRACTS, vol. 111, no. 11, 11 September 1989 Columbus, Ohio, US; abstract no. 92985, PORCELLINI, ADOLFO ET AL 'Limiting dilution analysis for detection of residual leukemic cells after bone marrow combined decontamination with mafosfamide followed by merocyanine-540-mediated photosensitization' see abstract & INT. J. CELL CLONING (1989), 7(4), 223-31 CODEN: IJCCE3; ISSN: 0737-1454, 1989 ---	1,5,6
Y	DATABASE BIOSIS BIOSCIENCES INFORMATION SERVICE, PHILADELPHIA, PA, US AN=93:22793, see abstract & 34TH ANNUAL MEETING OF THE AMERICAN SOCIETY FOR THERAPEUTIC RADIOLOGY AND ONCOLOGY, SAN DIEGO, CALIFORNIA, USA, INT. J. RADIAT. ONCOL. BIOL. PHYS., vol. 24, no. 1, 9 - 13 November 1992 page 207 WONG J.R. ET AL. 'A NOVEL METHOD OF PURGING CARCINOMA CONTAMINATED BONE MARROW USING THE LIPOPHILIC CATION RHODAMINE 123' ---	1-10
A	CHEMICAL ABSTRACTS, vol. 116, no. 15, 13 April 1992 Columbus, Ohio, US; abstract no. 147035, HAGHIGHAT, SHAGHAYEGH ET AL 'Laser dyes for experimental phototherapy of human cancer: comparison of three rhodamines' see abstract & LARYNGOSCOPE (1992), 102(1), 81-7 CODEN: LARYA8; ISSN: 0023-852X, 1992 ---	1-10
Y	CHEMICAL ABSTRACTS, vol. 116, no. 15, 13 April 1992 Columbus, Ohio, US; abstract no. 146920, BUNTING, JAMES R. 'A test of the singlet oxygen mechanism of cationic dye photosensitization of mitochondrial damage' see abstract	1-10
1 2 X	& PHOTOCHEM. PHOTOBIOLOG. (1992), 55(1), 81-7 CODEN: PHCBAP; ISSN: 0031-8655, 1992 ---	1

-/--

INTERNATIONAL SEARCH REPORT

Int. Application No.

PCT/CA 95/00485

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	CHEMICAL ABSTRACTS, vol. 112, no. 5, 29 January 1990 Columbus, Ohio, US; abstract no. 32723, GULLIYA, K. 'An in vitro model of autologous bone marrow purging for multiple myeloma and lung carcinoma cells by laser photoradiation therapy' see abstract & CANCER J. (1989), 2(11); 378-82 CODEN: CANJEI, 1989 ---	
X	DATABASE BEILSTEIN BEILSTEIN REGISTRY NUMBER=1334284, see abstract & ZH. ANAL. KHIM., vol. 15, 1960 page 523 KUONIZOW ET AL. ---	1
P,X	GB,A,2 283 744 (MOLECULAR PROBES INC) 17 May 1995 see claims -----	1

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☒ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
Remark: Although claims 3-10 are directed to a method of treatment of (diagnostic method practised on) the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.
2. ☐ Claims Nos.:
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

B x II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

INTERNATIONAL SEARCH REPORT

Information on patent family members

Int. Application No

PCI/CA 95/00485

Patent document
cited in search report

Publication
date

Patent family
member(s)

Publication
date

GB-A-2283744

17-05-95

US-A-

5459268

17-10-95

PATENT COOPERATION TREATY

PCT

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 10662-99PCT	FOR FURTHER ACTION see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/CA 00/ 01142	International filing date (day/month/year) 03/10/2000	(Earliest) Priority Date (day/month/year) 05/10/1999
Applicant UNIVERSITE DE MONTREAL		

This International Search Report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This International Search Report consists of a total of 3 sheets.

☒ It is also accompanied by a copy of each prior art document cited in this report.

1. Basis of the report

- a. With regard to the **language**, the international search was carried out on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

☐ the international search was carried out on the basis of a translation of the international application furnished to this Authority (Rule 23.1(b)).

- b. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application, the international search was carried out on the basis of the sequence listing :

☐ contained in the international application in written form.

☐ filed together with the international application in computer readable form.

☐ furnished subsequently to this Authority in written form.

☐ furnished subsequently to this Authority in computer readable form.

☐ the statement that the subsequently furnished written sequence listing does not go beyond the disclosure in the international application as filed has been furnished.

☐ the statement that the information recorded in computer readable form is identical to the written sequence listing has been furnished

2. ☐ **Certain claims were found unsearchable** (See Box I).

3. ☐ **Unity of invention is lacking** (see Box II).

4. With regard to the **title**,

☐ the text is approved as submitted by the applicant.

☒ the text has been established by this Authority to read as follows:

RHODAMINE DERIVATES FOR PHOTODYNAMIC DIAGNOSIS AND TREATMENT

5. With regard to the **abstract**,

☒ the text is approved as submitted by the applicant.

☐ the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.

6. The figure of the **drawings** to be published with the abstract is Figure No.

☐ as suggested by the applicant.

☐ because the applicant failed to suggest a figure.

☐ because this figure better characterizes the invention.

☒ None of the figures.

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/01142

A. CLASSIFICATION OF SUBJECT MATTER
IPC 7 A61K41/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHEDMinimum documentation searched (classification system followed by classification symbols)
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

CHEM ABS Data, EMBASE, BIOSIS, EPO-Internal, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	WO 93 00005 A (BAXTER INT ;QUADRA LOGIC TECH INC (CA)) 7 January 1993 (1993-01-07) claims 1-6	
Y	ADILI F ET AL: "HEMMUNG VON ALLOTRANSPLANTATABSTOSSUNG NACH PHOTODYNAMISCHER THERAPIE BIOLOGISCHER GEFAESSPROTHESEN" CHIRURGISCHES FORUM FUER EXPERIMENTELLE UND KLINISCHE FORSCHUNG,DE,BERLIN, no. SUPPL. 01, 1996, pages 271-274, XP000866003 ISSN: 0303-6227 the whole document	1-20
X	WO 96 07431 A (UNIV MONTREAL) 14 March 1996 (1996-03-14) claims	1-20

☒ Further documents are listed in the continuation of box C.☒ Patent family members are listed in annex.

* Special categories of cited documents:

- *A* document defining the general state of the art which is not considered to be of particular relevance
- *E* earlier document but published on or after the international filing date
- *L* document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)
- *O* document referring to an oral disclosure, use, exhibition or other means
- *P* document published prior to the international filing date but later than the priority date claimed

- *T* later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
- *X* document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
- *Y* document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.
- *G* document member of the same patent family

Date of the actual completion of the international search

26 January 2001

Date of mailing of the international search report

13/02/2001

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Berte, M

INTERNATIONAL SEARCH REPORT

International Application No

PCT/CA 00/01142

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	HESHMATI F ET AL: "EXTRACORPOREAL PHOTOCHEMOTHERAPY: A TREATMENT FOR ORGAN GRAFT REJECTION" THERAPEUTIC APHERESIS, US, BLACKWELL SCIENCE, MALDEN, MA, vol. 1, no. 2, 1997, pages 121-125, XP000866006 ISSN: 1091-6660	1
Y	the whole document	1-20
X	GUIMOND, M. (1) ET AL: "Specific elimination of anti-host T cell alloreactivity using a photodynamic approach." FASEB JOURNAL, (APRIL 20, 2000) VOL. 14, NO. 6, PP. A1074. PRINT. MEETING INFO.: JOINT ANNUAL MEETING OF THE AMERICAN ASSOCIATION OF IMMUNOLOGISTS AND THE CLINICAL IMMUNOLOGY SOCIETY SEATTLE, WASHINGTON, US MAY 12-16, 2000 , XP000979186 page 103.7	1-20
X	BRASSEUR, N. ET AL: "Eradication of multiple myeloma and breast cancer cells by TH9402-mediate photodynamic therapy: implication for clinical ex vivo purging of autologous stem cell transplants" PHOTOCHEM. PHOTOBIOLOG. (2000), 72(6), 780-787 , XP000979192 page 780, column 1 -column 2, paragraph 1	1-20
X	PAL, PRABIR ET AL: "Phototoxicity of some bromine-substituted rhodamine dyes: synthesis, photophysical properties and application as photosensitizers" PHOTOCHEM. PHOTOBIOLOG. (1996), 63(2), 161-8 , XP000979188 page 167, column 2 -page 168, column 1	1-20
X	VILLENEUVE, LUC: "Ex vivo photodynamic purging in chronic myelogenous leukemia and other neoplasias with rhodamine derivatives" BIOTECHNOL. APPL. BIOCHEM. (1999), 30(1), 1-17 , XP000979118 page 1, column 1	1-20

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

Continuation of Box I.1

Although claims 3-6 are directed to a method of treatment of the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

Although claim(s) 4-8 are directed to a diagnostic method practised on the human/animal body, the search has been carried out and based on the alleged effects of the compound/composition.

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/CA 00/01142

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9300005 A	07-01-1993	AU 650998 B AU 2257792 A CA 2089005 A,C DE 69221828 D DE 69221828 T EP 0544895 A ES 2110002 T JP 2811371 B JP 6500805 T MX 9203042 A US 5360734 A ZA 9204576 A	07-07-1994 25-01-1993 22-12-1992 02-10-1997 09-04-1998 09-06-1993 01-02-1998 15-10-1998 27-01-1994 01-07-1993 01-11-1994 31-03-1993
WO 9607431 A	14-03-1996	US 5556992 A AU 688100 B AU 3248895 A BR 9508779 A CA 2197435 A EP 0773794 A JP 10505349 T US 5773460 A	17-09-1996 05-03-1998 27-03-1996 23-12-1997 14-03-1996 21-05-1997 26-05-1998 30-06-1998